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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,130	02/20/2002	Richard B. Meagher	21099.0074U2	6995

23859 7590 03/04/2005

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EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HL

Office Action Summary	Application No.	Applicant(s)	
	10/079,130	MEAGHER ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,19-22 and 27-147* is/are pending in the application.

4a) Of the above claim(s) *35-41,43-111,122-129 and 139-147* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,19-22,27-34,42,112-121 and 130-138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/24/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 11/19/2004, is acknowledged.

Claims 18 and 23 – 26 have been cancelled.

Claims 1 – 17, 19 – 22, and 27 – 147 are pending.

2. Applicant's election of Group I (Claims 1 – 34, 42, 112 – 121, and 130 – 138, drawn to a hybridoma cell or a population of hybridoma cells) in the reply filed on 11/19/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant further provisionally elected the species of Igα, with traverse. The traversal is on the ground(s) that the number of species is not unreasonable. This is not found persuasive because the antibody receptors are patentably distinct, as their structures, physicochemical properties and/or mode of action are different, and they do not share a common structure that is disclosed to be essential for common utility. Furthermore, they require non-coextensive searches in the scientific literature. Therefore, each product is patentably distinct, and searching of these Inventions would impose an undue burden.

The requirement is still deemed proper and is therefore made FINAL.

However, in the interest of compact prosecution, the prior art search has been extended to include both species of antibody receptor.

The requirement for species election between the mutant forms of Igα and Igβ receptors has been obviated by cancellation of the respective claims.

3. Claims 35 – 41, 43 – 111, 122 – 129, and 139 – 147, drawn to non-elected inventions, are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions.

Claims 1 – 17, 19 – 22, 27 – 34, 42, 112 – 121, and 130 – 138 are under consideration in the instant application.

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth herein.

Upon review of the instant application, it is noted that the sequences disclosed at least in Figures 2 – 4 *are not accompanied by SEQ ID Numbers*. Applicant is reminded of the sequence rules which require a submission for all sequences of more than 9 nucleotides or 3 amino acids (see 37 CFR 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules. Applicant is reminded to amend the specification and the claims accordingly.

For sequences disclosed as part of the Drawings, the SEQ ID Numbers must be provided as part of the Brief Description of the Drawings.

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) in response to this Office Action.

5. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

However, the provisional application USSN 60/270,322 upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1 – 17, 19 – 22, 27 – 34, 42, 112 – 121, and 130 – 138 of this application.

Specifically, insufficient support was identified for the following limitations:

A population of hybridoma cells wherein greater than a specific percentage of cells expresses a monoclonal antibody that is bound to the cell surface, or a hybridoma cell wherein greater than a specific number or percentage of monoclonal antibody molecules are expressed on the cell surface – claims 1 – 16; and

A hybridoma cell comprising a vector or nucleic acid encoding Igα or Igβ – claims 17, 19 – 22, 28 – 34, 42, 112 – 121, and 130 – 138.

Consequently, the claims have been accorded the priority of the filing date of the instant application, i.e. 02/20/2002.

Should Applicant disagree with the Examiner's factual determination above, it is incumbent upon Applicant to provide a showing that specifically supports the instant claim limitations.

6. Applicant's IDS, filed 06/24/2004, is acknowledged, and has been considered.

7. The use of trademarks has been noted in this application (e.g. Zeocin on page 71). Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, e.g. on page 83. Applicant is required to

delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

9. The Drawings are objected to because of the following informality: The Brief Description of Figures refers to panels A, B, and C in figure 13, whereas Figure 13 does not have panels designated A, B, or C. Appropriate correction is required.

10. Claim 42 is objected to as being dependent on a non-elected claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 114 – 121 and 130 – 138 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 114 – 121 and 130 – 138 are indefinite in the recitation of "a population of hybridoma cells comprising a vector comprising a nucleic acid encoding Igα and/or Igβ that expresses monoclonal antibody," because it is unclear whether it is the population of hybridoma cells, the vector, or the nucleic acid that expresses the monoclonal antibody. Thus one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

B. Claims 114 – 121 and 130 – 138 are indefinite in the recitation of "fluorescence intensity of a population of cells," because it is unclear whether the measure of intensity refers to a mean, median, modal, or some other population-related

measure of fluorescence. Thus one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 8 – 9 and 117 – 119 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not provide a sufficient enabling description of the claimed invention.

The specification discloses that hybridoma cells expressing Igα and Igβ express about five times or ten times more antibody on the cell surface, as detected by fluorescence, than cells which do not express Igα and/or Igβ (pages 74 – 75 and Figures 11 and 13). The specification further discloses on page 2, last paragraph, that normal hybridoma cells in a population present approximately twenty antibody molecules on their surface.

The instant claims are directed a population of Igα/β expressing cells which have a 25-fold to 100-fold greater expression of antibody on cell surface, or which express greater than 250 or 500 antibody molecules on cell surface.

However, a person of skill in the art is not enabled to make and use hybridoma cells with the requisite properties without undue experimentation. For example, Parks et al. (of record, reference A76 on the IDS; see entire document) report that difficulties in fluorescent labeling antibody molecules on hybridoma cells are due to the very low levels of their surface expression (see entire document, in particular, e.g. page 1962 right column first paragraph). Therefore, the high levels of surface antibody expression cannot be readily accomplished without sufficient guidance. In the absence of such guidance, the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1 – 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Meilhoc et al. (of record, reference A59 on the IDS, see entire document).

Meilhoc et al. teach a population of hybridoma cells wherein at least 90% of cells express a monoclonal antibody on the cell surface (see entire document, in particular, page 170 and Figure 2; specifically, compare e.g. panels "11 hr" and "95 hr" in Figure 2).

Thus the reference teachings anticipate the claimed invention.

17. Claims 5 – 7, 10 – 13, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Maciak et al. (of record, reference A3 in the IDS, see entire document), as evidenced by the instant specification on page 2, last paragraph.

Maciak et al. teach a population of hybridoma cells with a higher than average density of monoclonal antibody on the cell surface (see entire document, in particular, e.g. column 1 paragraph 1). The instant specification clarifies on page 2, last paragraph, that the average density of surface antibody molecules on hybridoma cells is about 20.

Thus the reference teachings anticipate the claimed invention.

18. Claims 1 – 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Breitling et al. (German Patent DE19900635A1, see entire document).

Breitling et al. teach a method of producing hybridoma cells which express monoclonal antibody molecules on the surface of the cell (see entire document, in particular, e.g. the Abstract). Breitling et al. further teach hybridoma cells which express antibodies on the cell surface, as detected by FACS analysis (e.g. page 18 second paragraph of the translation): "hybridoma cells have a green fluorescence. This fluorescence is induced by the expression of antibodies on the cell surface of the hybridoma cells." The latter phrase indicates that all hybridoma cells express the antibody on their surface.

Thus the reference teachings anticipate the claimed invention.

19. Claims 5 – 7, 10 – 13, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Maciak et al. Breitling et al. (German Patent DE19900635A1, see entire document), as evidenced by the instant specification on page 2, last paragraph.

Breitling et al. have been discussed supra, and teach hybridoma cells which express antibodies on the cell surface, as detected by FACS analysis (e.g. page 18 second paragraph of the translation). The instant specification clarifies on page 2, last paragraph, that the "measurable" density of surface antibody molecules on hybridoma cells is about 20.

Thus the reference teachings anticipate the claimed invention.

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 1 – 7, 10 – 17, 19 – 22, 28 – 33, 42, 112 – 116, 120 – 121, and 130 – 138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matsuuchi (of record, reference A57 on the IDS, see entire document) in view of Maciak et al. (of record, reference A3 in the IDS, see entire document), as evidenced by the instant specification on page 2, last paragraph.

Matsuuchi et al. teach a method of expressing membrane-associated antibody by co-expressing Igα (alternative name MB-1) and Igβ with the antibody (see entire document, in particular, e.g. Abstract). The co-expression of Igα and Igβ leads to an approximately 10-fold increase in the cell surface expression of the antibody as detected by fluorescence, such that approximately 75% of cells expressing Igα and Igβ have at least two-fold greater fluorescence intensity than cells not expressing these receptors, and at least 10% of cells expressing Igα and Igβ have at least ten-fold greater fluorescence intensity than cells not expressing these receptors (Figure 1G, compare peak 3 with peaks 1 and 2).

The method taught by Matsuuchi et al. results in producing a cell comprising a vector, wherein the vector comprises nucleic acids encoding Igα and Igβ.

The instant specification clarifies on page 2, last paragraph, that the average measurable density of surface antibody molecules on hybridoma cells is about 20.

Matsuuchi et al. do not teach a hybridoma cell comprising a vector, wherein the vector comprises nucleic acids encoding Igα and Igβ.

Maciak et al. teach the importance of obtaining maximal yields of antibodies from hybridoma cultures, and that the yield is positively correlated with the surface expression of the antibody (see entire document, in particular, e.g. column 1 lines 25 – 30 and column 5, first paragraph).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Maciak et al. to those of Matsuuchi et al. to obtain the claimed hybridoma cell comprising a vector, wherein the vector comprises nucleic acids encoding Igα and Igβ.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, based on the teachings of Maciak et al. regarding importance of obtaining maximal yields of antibodies from hybridoma cultures. Ordinary artisan would have had a reasonable expectation of success, based on the teachings of Matsuuchi et al. that surface-bound expression of antibody molecules can be achieved by co-expressing them with Igα and Igβ molecules.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

22. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Matsuuchi et al. (of record, reference A57 on the IDS, see entire document) in view of Maciak et al. (of record, reference A3 in the IDS, see entire document), and further in view of Gossen et al. (US Patent 5,464,758; see entire document).

The combined references of Matsuuchi et al. in view of Maciak et al. have been discussed supra, and teach a hybridoma cell comprising a vector, wherein the vector comprises nucleic acids encoding Igα and Igβ.

The above references do not teach a hybridoma cell wherein nucleic acids encoding Igα and Igβ are linked to an inducible functional expression sequence.

However, it was well within the purview of an ordinary artisan at the time the invention was made place the respective sequences under the control of an inducible expression sequence, as evidenced e.g. by Gossen et al.

Gossen et al. teach an inducible expression system for expressing desired gene products in eukaryotic cells (see entire document, in particular, e.g. the Abstract), and review the advantages of inducible gene expression (see Background of the Invention in columns 1 – 2). Based on these advantages, an ordinary artisan would have been motivated, and would have a reasonable expectation of success, to link the Igα and Igβ sequences to an inducible functional expression sequence, e.g. as taught by Gossen et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

23. Conclusion: No claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644

February 14, 2005

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